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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LOEB, BRONWEN

ART UNIT PAPER NUMBER

1636

DATE MAILED: 03/26/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/556,390

Applicant(s)

YOUNG ET AL.

Examiner

Bronwen M. Loeb

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 58-69 is/are allowed.
- 6) ☒ Claim(s) 1-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 April 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This action is in response to the amendment filed 4 January 2002 in which claims 7, 23, 29, 39, 43, 44, 52, 58 and 64 were amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-69 are pending.

Claim Objections

1. Applicant is advised that should claim 52 be found allowable, claim 57 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

drop

Information Disclosure Statement

2. The information disclosure statement filed 28 July 2000 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

not done yet?

Nine of the references could not be located in this application or in either parent application. These references have therefore been crossed out on the attached Form

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1449. If copies of these nine references are provided in response to this action, they will be considered without a fee.

Response to Amendment

3. The rejection of claims 29-42, 44, 52 and 58-69 under 35 USC §112, second paragraph as being indefinite has been withdrawn in view of Applicant's amendment.

The rejection of claims 1-11, 13, 14, 29-39, 41 and 42 under 35 USC §103(a) as being unpatentable over Fields et al in view of any one of Erickson et al, Korsmeyer or Gallatin, and further in view of Wood has been withdrawn in view of Applicant's amendment.

The provisional rejection of claims 1-28 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 49-136 of copending Application 09/305,483 has been withdrawn in view of the issuance of 09/305,482 as USP 6,284,519.

4. New grounds of rejection are presented below.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 15-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 15 is vague and indefinite because it is unclear what selected phenotype based on the teachings in the specification is prevented by expression of the luciferase gene.

OK

Claim 16 is vague and indefinite in reciting "at least one of the endogenous nucleotide sequences is inactivated by reconstitution...". How does reconstitution inactivate a sequence? Should "reconstitution" be amended to "mutation"?

OK, first
new matter

Claim 29 recites the limitation "the selected phenotype" in step (ii) line 2. There is insufficient antecedent basis for this limitation in the claim.

OK

Claim 43 is vague and indefinite in reciting "a first heterologous fusion protein" in step (ii) a). Is this the same or different from the first heterologous fusion protein recited in step (i) a)?

OK

Claim 43 is vague and indefinite in reciting "a second heterologous fusion protein" in step (ii) b). Is this the same or different from the second heterologous fusion protein recited in step (i) b)?

OK

Claim 44 is vague and indefinite in reciting "at least one of the endogenous nucleotide sequences is inactivated by reconstitution...". How does reconstitution inactivate a sequence? Should "reconstitution" be amended to "mutation"?

OK, new
matter?

Claim 52 is vague and indefinite because it is unclear if these recitations are further limiting the recitations in claim 43 or ~~if~~ they are in addition to the recitations in claim 43.

cancelled,

Claim 52 is vague and indefinite in reciting "a first heterologous fusion protein" in step a). Is this the same or different from the first heterologous fusion protein recited in claim 43?

Claim 52 is vague and indefinite in reciting "a first peptide" in step a). Is this the same or different from the first peptide recited in claim 43?

Claim 52 is vague and indefinite in reciting "a second peptide" in step b). Is this the same or different from the second peptide recited in claim 43?

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. §102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. §122(b). Therefore, this application is examined under 35 U.S.C. §102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. §102(e)).

7. Claims 1, 4, 6, 7 and 14 are rejected under 35 U.S.C. §102(e) as being anticipated by Bachovin (USP 5,580,979). Bachovin teaches the yeast two hybrid assay according to Fields et al and disclose that luciferase can be used in the two

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hybrid assay as a reporter gene (col. 20, line 60- col. 21, line 19). One of the peptides of the peptide binding pair comprises an SH2 domain which recognize sequence-specific phosphorylated tyrosines in, for instance, growth-factor mediated signals, including PDGF (col. 1, line 40 – col. 2, line 44). The N-terminal domain of Gal4 (or a similar protein) is taught as the DNA binding domain and the C-terminal domain is taught as the transcriptional activation domain.

Claim Rejections - 35 USC § 103

8. Claims 1-8, 10, 11, 13, 14, 29-36, 38, 39, 41 and 42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Bachovin in view of Fields et al (USP 5,283,173) and Wood (USP 5, 641,641).

Bachovin is applied as above. Bachovin does not teach inactivation of an endogenous sequence; a peptide pair comprising a ligand and a receptor to which the ligand binds; expressing at least one heterologous fusion protein from an autonomously-replicating plasmid; any specific yeast strains'; or the two hybrid assay for testing a sample for binding to one or the other peptides of the peptide pair.

Fields et al teaches (see entire document) the yeast two hybrid system in which a first peptide of a binding pair is fused to the DNA binding domain of a transcriptional activation protein and the second peptide of a peptide binding pair is fused to the activation domain of a transcriptional activation protein and the binding of the two fusion proteins results in the expression of a reporter gene. The peptides of the binding pair can be any protein, including cell surface receptors and their ligands, such as growth

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factors (col. 3, lines 57-60). The yeast can be *Saccharomyces cerevisiae* or *Schizosaccharomyces pombe* (col. 6, lines 15-17). The transcriptional activation protein can be Gal4, Gcn4 or Adr1 (col. 4, lines 62-66). The host strain carries a deletion of the transcriptional activation protein (col. 6, lines 65-68). The fusion proteins can be expressed from autonomously-replicating plasmids (col. 5, lines 41-47).

Wood (entire document) provides detailed guidance on the use of luciferase, particularly Photinus luciferase, as a reporter gene in many cell types, including yeast. (It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute luciferase as a reporter gene into the yeast two hybrid assay of Fields et al, motivated by the teaching of Bachovin that luciferase can be used in the two hybrid assay and further motivated by Wood who teaches the ease with which luciferase can be assayed. One of ordinary skill in the art would reasonably expect that luciferase would function as a reporter gene in the yeast two hybrid assay based on the teachings of Bachovin which indicates the equivalence of different reporter genes in the two hybrid assay.

With respect to the rejections under 35 USC §103(a) set forth in the previous Office action and now withdrawn, Applicant argued that the Office mischaracterized the teachings of Wood and that Wood only teaches the use of luciferase as a report in assays involving extracts prepared from yeast cells. This is not persuasive because Wood does clearly encompass the in vivo use of the luciferase gene as a reporter gene. See for instance col. 5, lines 32-38 in which "genetic events in such sample (e.g. of

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cells)" is taught and col. 10, lines 57-64 which characterizes a preferred kit for assaying luciferase in cells.

9. Claims 1-11, 13, 14, 29-39, 41 and 42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Bachovin in view of Fields et al and Wood, as applied to claims 1-8, 10, 11, 13, 14, 29-36, 38, 39, 41 and 42 above, and further in view of one of Gallatin et al (USP 5,837,490) and Vojtek et al (Cell (1993) 74:205-214). Bachovin in view of Fields et al and Wood does not teach the use of LexA as the DNA binding domain in the yeast two hybrid assay. Gallatin et al (col. 8, lines 42-60) and Vojtek et al (p. 206 under Results) teach the use of LexA in the yeast two hybrid assay. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the DNA binding domain of LexA into the yeast two hybrid assay of Fields et al based on the teaching of Gallatin et al as to the equivalence of the LexA DNA binding domain and other DNA binding domains.

With respect to the rejections under 35 USC §103(a) set forth in the previous Office action and now withdrawn, Applicant argued that Gallatin et al was not a prior art document because the relevant disclosure was not part of series of applications until after the effective filing date of the instant specification. While this is true with respect to the teachings regarding luciferase, it is not true with respect to the use of the DNA binding domain of LexA in a two hybrid assay.

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Double Patenting

10. Claims 1-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-88 of U.S. Patent No. 6,284,519 in view of Bachovin (USP 5,580,979). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are drawn to yeast cells for use in a two hybrid assay and which comprise luciferase as a reporter gene, while the claims is USP 6,284,519 are drawn to the same yeast cell but encompassing any reporter gene. It would have been obvious to one of ordinary skill in the art to use luciferase as a reporter gene in a two hybrid assay since it is taught in the specification of USP 6,284,519, as well as in the prior art, as an equivalent reporter gene in the yeast two hybrid assay (see Bachovin, col. 20, line 60- col. 21, line 19).

Conclusion

Claims 58-69 are allowed. Claims 1-57 are rejected. Claims 12, 15-28, 40 and 43-69 are free of prior art.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as

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soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

March 25, 2002


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